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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/277,074	03/26/99	SHERMAN L	TSRI433.1DIV

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EXAMINER	
DAVIS,M	
ART UNIT	**PAPER NUMBER**
1642	12

DATE MAILED: 12/06/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/277074	
Examiner	**Group Art Unit**
	1642

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 (MONTH(S)) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 11/03/00.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disp sition of Claims

☒ Claim(s) 1, 47-50 is/are pending in the application.

Of the above claim(s) 47-50 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Acti n Summary

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

Applicant's election of group I, claim 1 in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

A telephonic conversation with Thomas Northrup on 10/06/00 results in election of SEQ ID NO:10.

It is noted that SEQ ID NO:10 constitutes a group, and **not a species**, as recited in the Office action of paper No:5, page 2, last paragraph, and page 3, wherein the Office action specifically recites that different sequences are patentably distinct because they are structurally distinct and because each sequence is a distinct epitope which could independently activate cytotoxic T cells.

The requirement is deemed proper and is therefore made FINAL.

Accordingly, claim 1, SEQ ID NO:10 is examined in the instant application.

SPECIFICATION

A corrected subtitute specification is required because the requested amendment to the specification to comply with sequence rule compliance, on 10/17/00, is extensive.

INFORMATION DISCLOSURE STATEMENT

The submitted information disclosure statement could not be examined, because all the patents recited in the PTO-1449 are missing.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The following is a quotation of the first paragraph of 35 USC 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Claim 1 is drawn to a polypeptide capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target malignant cells.

Although drawn specifically to the DNA art, the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly relevant to the instant rejected polypeptide. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

The specification discloses a peptide of SEQ ID NO:10, which could produce CTLs when injected into transgenic mice, wherein said CTLs could lysis some tumor cell lines *in vitro*. The claim encompasses any polypeptide capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target malignant cells. Thus the scope of the

claims includes numerous polypeptides with completely different structure. Structural features, that could distinguish the claimed polypeptide from those known in the art, are missing from the disclosure. No common structural attributes that identify the claimed polypeptides are disclosed. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the claimed polypeptides, SEQ ID NO:10 alone is insufficient to describe the claimed polypeptides. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of polypeptides. Thus, applicant was not in possession of the claimed polypeptides capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target malignant cells.

Thus, there is insufficient support of claim 1 as provided by the Interim Written Description Guidelines published in the June 5, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore, only an isolated polypeptide consisting of SEQ ID NO:10, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 is drawn to a polypeptide capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target malignant cells.

The specification discloses that injection of SEQ ID NO:10 (or H3 sequence) into transgenic mice A2.1/K^b xCD8, or A2.1 produces CTLs that could lyse some tumor cell lines that express both A2.1 and Her-2/neu. The specification contemplates the activation of CTLs for the treatment of cancer. Claim 1 encompasses a polypeptide capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target malignant cells *in vivo,* i.e., a polypeptide that could be used as a vaccine for treating animals or human patients with tumor burden.

One cannot extrapolate the teaching of the specification to the claimed invention because although the spleen cells of mice injected with the claimed peptide could be used to generate CTLs, none of these mice have a tumor burden, and the claimed CTLs produced are xenogeneic (specification, p.101). It is not clear how administration of the claimed peptide would produce a sufficient amount of CTLs to kill tumors in an animal or human that have malignant cells expressing both A2.1 and Her-2/neu. It is well known in the art that Her-2/neu is expressed at low level in normal tissue, i.e. a self-protein, and that self-tolerance may eliminate T cells that are capable of recognizing these epitopes with high avidity (Sherman, LA et al, 1998, Critical reviews

in Immunol, 18(1-2): 47-54). In other words, only CTLs with low affinity are left, which may not be optimal for tumor elimination *in vivo*. Further, even Applicant admits that there are a number of disadvantages to rely upon the immune system of the tumor-bearing host to provide CTLs (specification, p.101, second paragraph). One of the problem is that after some period of time in the presence of tumor cells, T cells may lose their functional activity.

In addition, one cannot extrapolate the teaching of the specification to the claimed invention because the specification provides no exemplification of or guidance on how to use the claimed vaccine formulation or antigen for active immunotherapy in humans. The goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. However, Ezzell (J. NIH Res, 1995, 7:46-49) reviews the current thinking in cancer vaccines and states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (see the entire document, particularly last paragraph) and further states that no one is very optimistic that a single peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (p 48, para 6). In addition, Spitler (Cancer Biotherapy, 1995, 10:1-3) recognizes the lack of predictability of the nature of the art when she states that "Ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: "cancer vaccines don't work". Ask a venture capitalist or the director of product development at a large pharmaceutical company and you're likely to get the same response." (p 1, para 1).

Furthermore, Boon (Adv Can Res, 1992, 58:177-210) teaches even if activated CTLs are significantly increased, the therapeutic success remains unpredictable due to inconsistencies in antigen expression or presentation by tumor cells (p.178, paragraph before last paragraph).

Moreover, it is well known that the art of anticancer drug discovery for cancer therapy is highly unpredictable, for example, Gura (Science, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second para). Because of the known unpredictability of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the claimed peptide would be useful for treating cancer. Further, the refractory nature of cancer to drugs is well known in the art. Jain (Sci. Am., 1994, 271:58-65) teaches that tumors resist penetration by drugs (p.58, col 1) and that scientists need to put expanded effort into uncovering the reasons why therapeutic agents that show encouraging promise in the laboratory often turn out to be ineffective in the treatment of common solid tumors (p. 65, col 3). Curti (Crit. Rev. in Oncology/Hematology, 1993, 14:29-39) teaches that solid tumors resist destruction by chemotherapy agents and that although strategies to overcome defense mechanisms of neoplastic cells have been developed and tested in a number of patients, success has been limited and further teaches that it is certainly possible that cancer cells possess many as yet undefined additional molecular mechanisms to defeat chemotherapy treatment

strategies and if this is true, designing effective chemotherapeutic regimens for solid tumors may prove a daunting task (para bridging pages 29-30) and concludes that knowledge about the physical barriers to drug delivery in tumors is a work in progress (p. 36, col 2). It is clear that based on the state of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the claimed peptide would be useful for treating cancer. In addition, Hartwell et al (Science, 1997, 278:1064-1068) teach that an effective chemotherapeutic must selectively kill tumor cells, that most anticancer drugs have been discovered by serendipity and that the molecular alterations that provide selective tumor cell killing are unknown and that even understanding the detailed molecular mechanism by which a drug acts often provides little insight into why the treated tumor cell dies (para bridging pages 1064-1065) and Jain (cited supra) specifically teaches that systemic treatment typically consists of chemotherapeutic drugs that are toxic to dividing cells (p. 58, col 2, para 2).

In addition, anti-tumor agents and those that prevent, reduce, retard or eliminate secretion of metastatic promoters, must accomplish several tasks to be effective. They must be delivered into the circulation that supplies the tumor or metastatic promotor producing cells and interact at the proper site of action and must do so at a sufficient concentration and for a sufficient period of time. It is clear, as disclosed above that the specification does not teach how to make/use a formulation with a targeting molecule. Also, the target cell must not have an alternate means of survival despite action at the proper site for the drug. In addition variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful

therapy. The formulation may be inactivated *in vivo* before producing a sufficient effect, for example, by degradation, immunological activation or due to an inherently short half life of the formulation. In addition, the formulation may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by fluids, cells and tissues where the formulation has no effect, circulation into the target area may be insufficient to carry the formulation and a large enough local concentration may not be established. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed methods with a reasonable expectation of success.

Further, the *in vitro* demonstration of CTL stimulated lysis of tumor cells lines cannot be correlated to the invention as claimed, because the CTLs are continously in contact with target cells in *in vitro* assays, and are not subjected to the denfense of the body. In addition, characteristics of cultured cell lines generally differ significantly from the characteristics of a primary tumor. Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teach that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in

homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences *In Vitro*). Further, Dermer (Bio/Technology, 1994, 12:320) teaches that, "petri dish cancer" is a poor representation of malignancy, with characteristics profoundly different from the human disease Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary -type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not, yet normal or malignant cells *in vivo* are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interations.Thus, based on the cell culture data presented in the specification, it could not be predicted that the claimed CTLs could kill malignant cells *in vivo*. The specification provides insufficient guidance with regard to theses issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which woul allow one of skill in the art to predict the efficacy of the claimed polypeptide in killing tumor cells *in vivo* with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed inventions with a reasonable expectation of success.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

1. If Applicant could overcome the above 112, first paragraph rejections, claim 1 is still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:10, capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo* in transgenic mice A2.1/K^b xCD8, or A2.1, wherein said CTLs specifically target malignant cells in tissue culture which express both A2.1 and Her-2/neu, does not reasonably provide enablement for any polypeptide capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target any malignant cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 1 is drawn to a polypeptide capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target malignant cells.

The specification discloses that injection of SEQ ID NO:10 (or H3 sequence) into transgenic mice A2.1/K^b xCD8, or A2.1 produces CTLs that could lyse some tumor cell lines that express both A2.1 and Her-2/neu. Claim 1, however, encompasses any polypeptide capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target any malignant cells.

One cannot extrapolate the teaching of the specification to the claimed invention because there is no guidance on or exemplification of any correlation between SEQ ID NO:10 and "any

polypeptide" capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target "any" malignant cells. The claim encompasses multitude numbers of peptides from different proteins that are capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target any malignant cells. The specification however does not disclose common structural attributes that identify the claimed polypeptides. There is insufficient guidance regarding the parameters and sequence of peptides which correlate with the ability to stimulate and generate CTLs. There is insufficient guidance regarding selection of peptides that meet the instant criteria of generating CTLs that kill tumor cells.

Furthermore, not any malignant cells would be a target for the claimed CTLs, because it is well known in the art that CTLs recognize and lyse a target cell only in the context of a complex of peptide-MHC class I, which is routed to the cell surface for expression, and potential recognition by specific TLCs, wherein the target cells should have the same subtype of HLA as CTLs (Grey, HM et al, 1994, WO 94/20127, page 1). The specification provides insufficient guidance with regard to theses issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which woul allow one of skill in the art to predict the efficacy of the claimed polypeptide in killing tumor cells *in vivo* with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed inventions with a reasonable expectation of success.

2. If Applicant could overcome the above 112, first paragraph rejections, claim 1 is still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:10, capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo* in transgenic mice A2.1/K^b xCD8, or A2.1, wherein said CTLs specifically target malignant cells in tissue culture which express both A2.1 and Her-2/neu, does not reasonably provide enablement for any polypeptide capable of specifically activating cytotoxic T lymphocytes (CTLs) in a human patient, wherein said CTLs specifically target any malignant cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 1 is drawn to a polypeptide capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target malignant cells.

The specification discloses that injection of SEQ ID NO:10 (or H3 sequence) into transgenic mice A2.1/K^b xCD8, or A2.1 produces CTLs that could lyse some tumor cell lines that express both A2.1 and Her-2/neu. In other words, the CTLs are xenogeneic (specification, p. 101). Claim 1, however, encompasses polypeptide capable of specifically activating cytotoxic T lymphocytes (CTLs) in a human patient having tumors expressing A2.1 and Her-2/neu, wherein said CTLs specifically target any malignant cells.

One cannot extrapolate the teaching of the specification to the claimed invention, because it is well known in the art that Her-2/neu is expressed at low level in normal tissue, i.e. a self-protein, and that self-tolerance may eliminate T cells that are capable of recognizing these

epitopes with high avidity (Sherman, LA et al, 1998, Critical reviews in Immunol, 18(1-2): 47-54). In other words, only CTLs with low affinity are left, which may not be optimal for tumor elimination *in vivo*. Further, even Applicant admits that there are a number of disadvantages to rely upon the immune system of the tumor-bearing host to provide CTLs (specification, p.101, second paragraph). One of the problem is that after some period of time in the presence of tumor cells, T cells may lose their functional activity. Thus it is unpredictable that injection of SEQ ID NO:10 into a human patient having tumors expressing A2.1 and Her-2/neu would produce and activate a significant amount of specific CTLs. The specification provides insufficient guidance with regard to theses issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which woul allow one of skill in the art to predict the efficacy of the claimed polypeptide in killing tumor cells *in vivo* with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed inventions with a reasonable expectation of success.

REJECTION UNDER 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Grey, HM et al, 1994, WO 94/20127, as evidenced by Engleman et al, PN=4,950,598.

Claim 1 is drawn to a polypeptide capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target malignant cells.

Grey et al teach peptides that could induce the production of specific CTLs in transgenic mice, which lyse peptide-coated targets cells Jurkat which express the A2 KB molecule (p.76 and table 24).

It is well known in the art that Jurkat cells are human leukemia cell lines (Engleman et al, column 3, second paragraph). In other words, Jurkat cells are malignant cells.

Thus the peptides taught by Grey et al are the same as the claimed polypeptide, which could induce the production of specific CTLs in transgenic mice, wherein said CTLs lyse target Jurkat cells, which are inherently leukemia cell lines.

2. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Grey, HM et al, 1994, WO 94/20127, or Cheever et al, PN=5,726,023.

Claim 1 is drawn to a polypeptide capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target malignant cells.

Grey et al teach a sequence KIFGSLAFL (table 25, page 80, first sequence), which is the same as the claimed SEQ ID NO:10.

Cheever et al teach a sequence, SEQ ID NO:27 (column 39) which is the same as the claimed SEQ ID NO:10.

Thus the sequences taught by Grey et al and Cheever et al would have the same properties and characteristic of the claimed SEQ ID NO:10, i.e. capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target malignant cells. The references do not specifically teach that the recited peptide sequences are capable of specifically activating cytotoxic T lymphocytes (CTLs) *in vivo*, wherein said CTLs specifically target malignant cells. However, the claimed peptide sequence appears to be the same as the prior art peptide sequences, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable diffrences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Minh-Tam B. Davis whose telephone number is (703) 305-2008. The examiner can normally be reached on Monday-Friday from 9:30am to 3:30pm, except on Wesnesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached on (703) 308-3995. The fax phone number for this Group is (703) 308-4227.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0916.

Minh-Tam B. Davis

November 27, 2000

SUSAN UNGAR, PH.D
PRIMARY EXAMINER